Accepted author's manuscript. Published in final edited form as: American Journal of Medicine 2021; 134(1): e71.
Publisher DOI: 10.1016/j.amjmed.2020.09.008

The Reply

Dr. Modarressi suggests in his letter that our interpretation of the TRUST study[1] needs caution because patients who had a thyroid-stimulating hormone (TSH) level between 4.6 and 6.9 mIU/L could be physiologically euthyroid. We disagree and provide 3 specific points in response.

When we designed the TRUST trial, we chose to set a TSH target of 0.40-4.59 mIU/L with levothyroxine treatment, which was the range used to define euthyroidism in the Thyroid Studies Collaboration[2] and contemporary guidelines,[3] despite the current discussion of using an age-specific reference.[4]

We enrolled only participants who had persistent elevated TSH levels (4.60-19.99 mIU/L).[1,5] The TSH value was required to be within the eligibility window on at least 2 occasions that were 3 months to 3 years apart. In the TRUST trial, among the 2647 older adults screened for eligibility, 1645 did meet inclusion criteria because of a reversion of TSH level.[5] The TSH levels among participants randomized in the placebo group remained elevated over the study period (5.29 mIU/L in average).[1] Therefore, we can assume that participants who were truly euthyroid were not studied in the TRUST trial.

The proportion of older participants with TSH ≥7 mIU/L in our study (23.8%) was representative, as the prevalence of such abnormality at this age category accounts for about 10% of the elderly population.[4] In our study, prespecified stratification according to baseline TSH levels (4.6-6.9, 7.0- 9.9, ≥10 mIU/L) yielded similar results without statistical interactions.[1] These findings were replicated in another trial of patients with subclinical hypothyroidism where levothyroxine compared with placebo had no impact on cardiac function.[6] Because the vast majority of patients treated for subclinical hypothyroidism in practice have a TSH value between 4.6 and 6.9 mIU/L,[4] the inclusion of those participants enabled us to evaluate the treatment effect of levothyroxine in this key subgroup.

Although we agree that age-specific reference for the diagnosis of subclinical hypothyroidism in the elderly needs to be re-discussed,[4] current findings found no benefits of levothyroxine on cardiac function among older adults with subclinical hypothyroidism, including among those with TSH ≥7 mIU/L.[1,6]

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Funding: None.
Conflict of Interest: NR's research was supported by grants from the Swiss National Science Foundation (SNSF 320030-150025 and 320030-172676), and investigator-driven grants from the Velux Stiftung (974a, to NR) and the Swiss Heart Foundation (to NR). The TRUST Trial was supported by a research grant (grant agreement number 278148) from the European Union FP7-HEALTH-2011 program). No disclosures for other authors.
Authorship: All authors have participated in the preparation of the manuscript.
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